

WHAT IS CLAIMED IS:

1. An adenovirus packaging cell line permissive for replication of an E1A/E1B deficient adenovirus vector, wherein said cell line comprises an adenovirus E1A coding sequence and an adenovirus E1B coding sequence operably linked to a promoter that lacks substantial sequence identity with a native adenovirus E1A or E1B promoter.
2. The adenovirus packaging cell line of Claim 1, wherein said adenovirus E1A coding sequence and said adenovirus E1B coding sequence are stably integrated into said cell line.
3. The adenovirus packaging cell line of Claim 2, wherein said adenovirus E1A coding sequence and said adenovirus E1B coding sequence are operably linked to identical promoters.
4. The adenovirus packaging cell line of Claim 2, wherein said adenovirus E1A coding sequence and said adenovirus E1B coding sequence are operably linked to the same promoter.
5. The adenovirus packaging cell line of Claim 2, wherein said adenovirus E1A coding sequence and said adenovirus E1B coding sequence are operably linked to different promoters.
6. The adenovirus packaging cell line of Claim 5, wherein said adenovirus E1A coding sequence and said adenovirus E1B coding sequence are stably integrated at different sites in said cell line.
7. The adenovirus packaging cell line of Claim 6, wherein said cell line is a human cell line.
8. The adenovirus packaging cell line of Claim 7, wherein said cell line is selected from the group consisting of A549 cells permissive for adenovirus replication PC-3 cells or primary cells permissive for adenovirus production.

9. The adenovirus packaging cell line of Claim 1, wherein said promoter that lacks substantial sequence identity with a native adenovirus E1A or E1B promoter is a constitutive promoter.

10. The adenovirus packaging cell line of Claim 1, wherein said promoter that lacks substantial sequence identity with a native adenovirus E1A or E1B promoter is a regulatable promoter.

11. The adenovirus packaging cell line of Claim 9, wherein said promoter is a retrovirus promoter.

12. The adenovirus packaging cell line of Claim 1, wherein said adenovirus E1A coding sequence encodes an adenovirus 243 gene product; 289 gene product, or both 243 and 289 gene product.

13. The adenovirus packaging cell line of Claim 12, wherein said adenovirus E1A coding sequence comprises the sequence set forth in SEQ ID NO:1.

14. The adenovirus packaging cell line of Claim 1, wherein said adenovirus E1B coding sequence encodes adenovirus 19 Kd gene product; 55 Kd gene product, or both 19 and 55 Kd gene product.

15. The adenovirus packaging cell line of Claim 14, wherein said adenovirus E1B coding sequence comprises the sequence set forth in SEQ ID NO:4.

16. An adenovirus packaging cell line comprising a first expression vector and a second expression vector stably integrated into the genome of said cell line, wherein said first vector comprises adenovirus E1A coding sequences, operatively linked to a non-adenoviral heterologous promoter, and said second vector comprises adenovirus E1B coding sequences operatively linked to a non-adenoviral heterologous promoter.

17. A method of producing an adenovirus packaging cell line permissive for replication of an E1A/E1B deficient adenovirus vector, the method comprising:

introducing into a cell line permissive for adenovirus replication, an expression vector comprising (i) an adenovirus E1A coding sequence operably linked to a promoter that lacks substantial sequence identity with a native adenovirus E1A or E1B promoter and (ii) an adenovirus E1B coding sequence operably linked to a promoter that lacks substantial sequence identity with a native adenovirus E1A or E1B promoter.

18. The method according to Claim 17, wherein said adenovirus E1A coding sequence and said adenovirus E1B coding sequence are present on separate vectors.

19. The method according to Claim 17, wherein said adenovirus E1A coding sequence and said adenovirus E1B coding sequence are present on the same vector.

20. The method according to Claim 17, wherein said E1A expression vector is a retroviral expression vector.

21. The method according to Claim 17, wherein said E1B expression vector is a retroviral expression vector.

22. The method according to Claim 17, wherein both said E1A and E1B expression vectors are retroviral expression vectors.

23. A method of producing E1A/E1B deficient adenovirus, the method comprising:
introducing an E1A/E1B deficient adenovirus into the packaging cell line of claim 1;
and

recovering from said cell line a population of adenovirus substantially free of
replication competent adenovirus.